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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,383	06/26/2006	Kyu Hyun Lee	5804900032	3667

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EXAMINER	
HIRIYANNA, KELAGINAMANE T	
ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,383	LEE ET AL.	
	Examiner	Art Unit	
	Kelaginamane T. Hiriyanna	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 06/21/2007 in response to office action mailed on 01/24/2007 has been acknowledged.

Claims 1-23 are amended.

Claims 1-23 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action. Declarations filed by one of the applicants under 37 C.F.R § 1.132 are duly considered.

Claim Rejections - 35 USC § 101

Claims 1-23 stand rejected under 35 U.S.C. 101 because claim is drawn to non-statutory subject matter for the reason of record as set forth in the previous office action mailed on 01/24/2007.

Response to Arguments of 06/21/2007:

Applicant argues that an amendment to the claims indicating cells as containing a gene encoding 'a recombinant protein' should overcome the rejection.

Applicants arguments however, found not persuasive because "cells" as recited encompass cells as they are naturally present inside the body in vivo and cannot be part of the pharmaceutical composition. Hence the rejection is maintained. The insertion of a phrase such as 'an isolated host cell', or 'a cultured mammalian/or human cell' or 'cell of a non-human mammal' or 'excluding human organism' would overcome this rejection.

Claim Rejections - 35 USC § 112

Claims *1-16* are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The scope of invention as claimed encompasses compositions of any gene carriers or any cells (of any tissue, derived from any tissue, autologous, allogenic, xenogenic etc.) harboring a human gene encoding a recombinant protein consisting of human apliporotein(a) kringle KIV9-KIV10-KV (LK68) or KV (LK8) as the pharmaceutical composition for treating any solid tumor or metastasis thereof.

The specification at best teaches compositions comprising LK68 and LK8 gene variants represented by SEQ ID NO:1 or SEQ ID NO:2 of in expression vectors capable of expressing the corresponding gene products.

The application does not disclose pharmaceutical compositions comprising any other variants of the gene apliporotein(a) kringle KIV9-KIV10-KV (LK68) or KV (LK8) genes other than SEQ ID NO:1 or SEQ ID NO:2.

Thus the number of examples of gene carriers, cells and the variants of the therapeutic gene provided does not commensurate with the scope and breadth of instant claims.

Applicant is referred to the guidelines for ***Written Description Requirement*** published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110 (see <http://www.uspto.gov>). The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (See In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In analyzing whether the written description requirement is met for the genus claim, it is first determined whether a representative number of species have been described by their complete structure. Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. conserved motifs or domains).

Since the specification fails to disclose other claimed compositions that contained sufficient number of examples of variants of apliporotein(a) kringle KIV9-KIV10-KV (LK68) or KV (LK8), it is not possible to envision the broadly claimed compositions would provide the same therapeutic results as SEQ ID NO:1 or SEQ ID NO:2. One cannot describe what one has not conceived. (See Fiddes v. Baird, 30 USP2d 1481 at 1483). Therefore, the lack of disclosure in the specification is not deemed sufficient to reasonably convey to one skilled in the art that the applicants were in possessions of the huge genera recited in the claims at the time the application was filed. Furthermore the possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In the instant case the compositions as claimed has been defined only by a statement of homology that encompasses any variants of apliporotein(a) kringle KIV9-KIV10-KV (LK68) or KV (LK8) in any cells which conveyed no distinguishing information about the identity of the broadly claimed species of therapeutic gene or the cells or the gene carriers. Accordingly one of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of a single member of this genus would not be representative of claimed genus of gene variants, cells or gene carriers and is insufficient to support the claim in its present scope. A gene is a hereditary unit that occupies a specific location on a chromosome and determines a particular characteristic in an organism. The art does not provide an accepted definition of 'gene" and elaboration of its characteristic. The claims under consideration read upon a gene, which lack an adequate written description in the absence of specific and particular disclosure of the "gene" characteristics. At the best the specification provides an description of compositions comprising "human apolipoprotein(a) gene segments with nucleotide

sequence represented in SEQ ID NO:1 or SEQ ID NO:2 and encoding KIV9-KIV10-KV (LK68).

Claims 1-17 and 22-23 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition comprising nucleotide sequence represented in SEQ ID NO: 1 or SEQ ID NO:2 in an plasmid or an adeno-associated viral vector (rAAV), is not enabled for any variant of apliporotein(a) gene segment encoding kringle KIV9-KIV10-KV(LK-68) or KV(LK8. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 18-21 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating tumors using pharmaceutical compositions comprising a plasmid or an adeno-associated viral vector (rAAV) as gene carrier capable of expressing a nucleotide sequence represented in SEQ ID NO: 1 or SEQ ID NO:2 encoding and capable of expressing a variant of apliporotein(a) kringle KIV9-KIV10-KV wherein the said gene carriers are administered by direct intramuscular injections and wherein the polypeptide encoded by said nucleotide sequences act in vivo as anti-angiogenic factors that inhibit the growth of a solid tumor or their metastasis thereof, does not enable any sequence variants of said apliporotein(a) kringle gene or any gene carriers or any cells or any method of administration. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Response to both the above rejections are addressed below:

Response to Arguments of 06/21/2007: Applicant argues and files 37 C.F.R 1.132 declarations to support the breadth of instant claims for using both plasmid and AAV vectors. Applicant further argues that application should considered enabling for the inventions as claimed with regard to cell and gene therapy of the solid tumors and metastasis there of.

The applicants' argument and supporting statements regarding gene carriers have been found persuasive as to extend the inclusion of plasmid vectors and AAV vectors as gene carriers. The applicants arguments are however, found not persuasive regarding the breadth of the claims regarding use of any variants of gene encoding apliporotein(a) kringle KIV9-KIV10-KV and use of any cell (recombinant) for treating tumors and metastasis there of because the specification fails to disclose enabled pharmaceutical compositions and a method of treating tumors using compositions other than those comprising a plasmid or an adeno-associated viral vector (rAAV) as gene carrier capable of expressing a nucleotide sequence represented in SEQ ID NO:1 or SEQ ID NO:2 encoding and capable of expressing apliporotein(a) kringle KIV9-KIV10-KV, it does not enable one skilled in the art to practice the invention as claimed without further undue amount of experimentation, which requires testing of all the variants of said sequences in gene carriers or cells with gene carriers for therapeutic effect on sufficient number of solid tumors or metastasis thereof. At issue, under the enablement requirement of 35 U.S.C. 112, first paragraph is whether, given the Wands-factors, the experimentation was undue or unreasonable under the circumstances. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See Fields v. Conover, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970) for the reason of record as set forth in the previous office action mailed on 01/24/2007. Hence the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, and 8-10 are rejected under 35 USC 102 (b) as being anticipated by Chang et al., (WO 01/19868).

The above claims are directed to a pharmaceutical composition containing a gene carrier or cell harboring human apolipoprotein kringle KIV9-KIV10-KV (LK68) or

KV (LK8) and in further limitations carrier is a vector or a recombinant virus and the cells harboring vector including hematopoietic stem cells, dendritic cells and to a method of for the prevention or the treatment of a solid tumor including its growth or metastasis by administering said gene carrier.

Regarding claims 1-4, 8-10 Chang teaches compositions comprising vectors with nucleotide sequences encoding human apolipoprotein kringle KIV9-KIV10-KV (LK68) or KV (LK8) (Abstract, p.1, lines 8-17, p.4, lines 27-36 bridging p.5). Chang further teaches that proteins encoded by said sequences as anticancer agents and inhibit angiogenesis (Abstract), p.3, lines 10-37 bridging p.4-5) and they inhibit endothelial cell proliferation, migration and suppress lung carcinoma (p.15, lines 10-35 bridging p.16-20). The cited art thus anticipates the invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6 and 18-21 are rejected under 35 USC 103 (a) as being unpatentable over Chang et al (WO 01/19868 A1) applied to claims 1-4, and 8-10 as above and further in view of Trieu et. al (1999, Biochem. Boiphys. Res. Comm. 257: 714-718).

The above claims are directed to a pharmaceutical composition containing a gene carrier or cell harboring human apolipoprotein kringle KIV9-KIV10-KV (LK68) or KV (LK8) and in further limitations carrier is a vector or a recombinant virus and the cells harboring vector including hematopoietic stem cells, dendritic cells and to a method of for the prevention or the treatment of a solid tumor including its growth or metastasis by administering said gene carrier.

Regarding claims 1-4, and 8-10 Chang teaches compositions comprising vectors with nucleotide sequences encoding human apolipoprotein kringle KIV9-KIV10-KV (LK68) or KV (LK8) (Abstract, p.1, lines 8-17, p.4, lines 27-36 bridging p.5). Chang further teaches that proteins encoded by said sequences as anticancer agents and inhibit

angiogenesis (Abstract), p.3, lines 10-37 bridging p.4-5) and they inhibit endothelial cell proliferation, migration and suppress lung carcinoma (p.15, lines 10-35 bridging p.16-20). Chang however does not teach a composition comprising tumor cells and a method of treating tumors by administering nucleic acids into any animals.

Regarding claims 1-4, 8-10 and 18-21 Trieu teaches that there is an established link between cancer and Apo(a) (the protein that contains KIV9-KIV10-KV (LK68) or KV (LK8)) levels and a method of treating Lewis lung carcinoma (LL/2) cancer wherein the cancer cells show a delayed growth of tumor and reduced angiogenesis when provided with apo(a) transgene (Abstract and entire article). Regarding claim 6 Trieu teaches providing CHO-K1 cells over expressing truncated human apo(a) transfected using a vector. Trieu further teaches full length recombinant apo(a) causes tumor suppression (p.714, abstract, col.2, 1st paragraph, 3rd paragraph; p.715, col.1 3rd paragraph, col.2, 1st paragraph; p.716, Fig.2). Trieu additionally teaches that a further characterization of structural components of apo(a) responsible for its previously unappreciated anti-tumor effects may provide the basis for novel and effective cancer treatment methods that employ apo(a) fragment or functional analogs of apo(a) as inhibitors of tumor angiogenesis. Trieu however, does not particularly teach the limitation of using gene coding for Apo(a) protein fragments that contains KIV9-KIV10-KV (LK68) or KV (LK8) as a tumor therapeutic agent.

Thus it would have been obvious to one of skill in the art to replace the full length apo(a) fragment in the gene therapeutic vector construct of Trieu to substitute fragment of apo(a) gene that codes for LK68 and LK8 kringles and treat a solid tumor or metastasis of thereof. One of the skill in the art would be motivated to use the gene fragment that codes for LK68 and LK8 kringles as it increases the efficacy of tumor gene therapy while simplifying the effort of dealing with the full length gene and gene product. One of skill in the art would have an expectation of success of making and using a pharmaceutical composition for gene therapy of tumors using gene coding sequences for kringles KIV9-KIV10-KV (LK68) or KV (LK8) as sub-cloning of gene fragments in therapeutic vectors and their therapeutic use is routine in the art of gene therapy. Thus the invention as claimed would have been *prima facie* obvious to one of skill in the art.

Conclusion:

No claim allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanna Ph.D.*, whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Friday from 9 AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach Ph.D.*, may be reached at **(571) 272-0739.** The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

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